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| 09/981,271 | 10/17/2001 | Samuel Achilefu | MRD-72 | 6423 |

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EXAMINER

JONES, DAMERON

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1616

8

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/981,271

Applicant(s)

ACHILEFU ET AL.

Examiner

D. L. Jones

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2001 and 05 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 3-7 and 10-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,8,9,15-17,20 and 21 is/are rejected.
- 7) ☒ Claim(s) 18,19 and 22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5. 6) ☐ Other:

Art Unit: 1616

ACKNOWLEDGMENTS

1. The Examiner acknowledges Paper No. 7., filed 3/5/03, wherein the specification and claims 1 and 8 were amended.

Note: Claims 1-22 are pending.

APPLICANT'S INVENTION

2. Applicant's invention is directed to tumor targeted photodiagnostic and phototherapeutic agents and uses thereof.

ACKNOWLEDGMENT OF APPLICANT'S ELECTION

3. Applicant's election with traverse of Group I (claims 1-22) directed to Formula 1 wherein both W1 and W2 are CR10R11 in Paper No. 7, filed 3/5/03, is acknowledged. In addition, the Examiner acknowledges the election of the species of Formula 1 wherein W1 and W2 = CR10R11; Y1, Y2, Z1, and Z2 = (CH₂)_a-CONH-Bm; X1 and X2 = N; Q = O; K1 and K2 = CH₂; R1-R9 = H; and R10 and R11 = CH₃. The traversal is on the ground(s) that the basis of the restriction is improper since all the claims are directed to Formula 1 and have the same utility. This is found non-persuasive for reasons of record in the office action mailed 2/4/03, Paper No. 6, and because depending upon the assigned value of the variables (e.g., W1 and W2) of Formula 1, the core structure varies from one group of species to another. Hence, a separate search and consideration of the prior art is necessary. Thus, the restriction requirement is still deemed proper and is therefore made FINAL.

Art Unit: 1616

Note: It should be noted that initially Applicant's elected species was searched. However, since no prior art was found which could be used to reject the claims, the search was expanded to the species wherein W1 and W2 = CR10R11; R10 and R11 = CH3; R1-R9 = H; K1 and K2 = (CH2)3; X1 and X2 = N; Y1, Y2, Z1, and Z2 = H; a1 = 3; b1 = 0; and Q = single bond (this species will be referred to as EXP#1).

WITHDRAWN CLAIMS

4. Claims 3-7 and 10-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

102 REJECTION

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Hasan et al (Journal of Controlled Release, 10 (1989), 107-117).

Hasan et al disclose monoclonal antibody chromophore conjugates that are selective phototoxins (see entire document, especially, abstract). In particular, Hasan et al disclose tetramethylindotricarbocyanine (TCCC, see page 108, Figure 1(b)) that fulfills the requirements of Applicant's compound claims when W1 and W2 = CR10R11;

Art Unit: 1616

R10 and R11 = CH₃; R1-R9 = H; K1 and K2 = (CH₂)₃; X1 and X2 = N; Y1, Y2, Z1, and Z2 = H; a1 = 3; b1 = 0; and Q = single bond (this species will be referred to as EXP#1).

In addition, Hasan et al disclose that the chromophores are active when illuminated, so it is not necessary for the conjugate to be completely tumor selective (page 108, column 1, first complete paragraph). The Mab-conjugates are prepared using a spacer arm in which the chromophore is bound to a polymer which is then linked to the Mab (pages 109-110, bridging paragraph). In vitro cytotoxic potential of the conjugate was evaluated by its potential to selectively kill target cells (page 111, column 2, first complete paragraph). TCC was prepared and characterized. The absorption spectrum showed a maximum at 739 nm in PBS and 745 nm in MeOH (page 111, column 2, second complete paragraph). In the discussion section of Hasan et al, it is disclosed that a cyanine chromophore, TCC, was conjugated via a polymer (PGA) to two Mabs and that PGA is known to be useful in combination with Mabs as a carrier for drugs and toxins. Furthermore, it is disclosed that the efforts of Hasan et al include systematically evaluating a variety of chromophores and carrier polymers as potential photochemotherapeutic agents and as investigational tools for photobiologic mechanisms (page 115, column 1, first complete paragraph). Also, it is disclosed that the fact that non-target cells treated similarly were unaffected affirms the selectivity of the conjugate and suggests that the conjugate might be useful in photochemotherapy (page 116, column 1, first complete paragraph). Finally, Hasan et al disclose that the detailed characterization of the conjugate may result in preparation of more effective

Art Unit: 1616

conjugates and that their lab is studying in vivo applications of the conjugate (page 116, column 1, second complete paragraph).

Thus, both Applicant and Hasan et al disclose a compound encompassed by Applicant's Formula 1.

103 REJECTIONS

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1, 2, 8, 9, 15-17, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hasan et al (Journal of Controlled Release, 10 (1989), 107-117).

DA Hasan et al (see discussion above) fail to disclose administering TCC to a subject and to ^{show} should compounds wherein R10 and R11 = C2 - C10 alkyl.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Hasan et al and administer TCC to a subject because Hasan et al disclose that the detailed characterization of the conjugate may result in preparation of more effective conjugates and that their lab is studying in vivo applications of the conjugate (page 116, column 1, second complete paragraph).

It would have been obvious to one of ordinary skill at the time the invention was made to use other structurally similar compounds wherein R10 and R11 are C2 - C10

Art Unit: 1616

alkyl because a skilled practitioner in the art would recognize that a homologous series is a family of chemically related compounds that vary from member to member by a CH₂ group. Hence, a practitioner would know that the characteristics normally possessed by members of a homologous series are principally the same. Thus, varying gradually from member to member, a chemists knowing the properties of one member of a series would in general know what to expect in adjacent members. As a result, a mere difference in degree is not the marked superiority which will ordinarily remove the unpatentability of adjacent homologues of old substances.

CLAIM OBJECTIONS

9. Claims 18, 19, and 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Note: The claims are distinguished over the prior art of record because the prior art neither anticipates nor renders obvious the additional limitations present in the dependent claims. In addition, it should be noted that the search has not been extended beyond the elected species and the expanded species (EXP #1) as set forth above.

COMMENTS/NOTES

10. The Examiner is aware of numerous applications filed by Applicant which contain similar subject matter. Thus, while the Examiner has searched pending applications


Art Unit: 1616

and patented files for double patenting, some applications may have been inadvertently missed. Hence, the Examiner respectfully requests that Applicant submit serial numbers of cases, now pending or newly filed, which contain overlapping or related subject matter.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640. The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose' Dees can be reached on (703) 308- 4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



D. L. Jones
Primary Examiner
Art Unit 1616

May 16, 2003